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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,858	GISH ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-58 and 61-70* is/are pending in the application.

4a) Of the above claim(s) *13-55, 68-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,56-58 and 61-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 4-5, 59-60.

Accordingly, claims 1-3, 6-12, 56-58, 61-67 are examined in the instant application.

The following are the remaining rejections.

OBJECTION

1) The specification is objected to because tables 15-16, recited in original claims 1-70, are not found in the specification.

Further, in the communication of 07/16/04, Applicant submits an amendment of the specification, in which table 11 at the beginning on page 302 of the specification is amended as Table 16.

The amendment cannot be considered and is not entered.

It is noted that the specification does not have page 302. The submitted specification has only 295 pages. The claims are at pages 428-435. The abstract is at page 436. Pages 296-427 seem to be missing.

2) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 39, line 13 .

Applicant is required to check the entire disclosure and delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP 608.01 .

Appropriate correction is required.

3) The Oath or Declaration submitted on 08/21/03 is objected to, due to the amendment of the continuation data on 07/16/04, claiming priority as "a continuation-in-part" of SN 09/847046, 09/733288, 09/687576, and 09/733742. The Oath or Declaration however does not claim benefit under 35 USC 120 of these applications.

A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP § § 602.01 and 602.02.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 1-3, 6-12, 56-58, 61-67 are rejected under 112, second paragraph, for omitting essential steps of detecting or quantifying the hybridizing complex, and correlate the results with the preamble, in claims 1 and 56 respectively, for reasons already of record in paper of 07/15/05.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

The claimed method only has the initial step of "contacting".

The essential steps of "detecting" or "quantifying" in claims 1 and 56, respectively, are still omitted.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-3, 6-12, 56-58, 61-67 are rejected under 112, first paragraph, pertaining to lack of a clear written description of a polynucleotide that "selectively hybridizes" to a nucleic acid encoding SEQ ID NO:42, the nucleotide sequence SEQ ID NO:41, a sequence at least "80% or 95% identical to SEQ ID NO:41", or a nucleic acid "comprising" a sequence "complementary" to SEQ ID NO:41, for reasons already of record in paper of 07/15/05.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

Rejection remains, because the amendment does not address this issue.

The specification and the claims do not meet the 112, first paragraph, written description requirement for the following reasons:

1) Due to the language "selectively hybridizes", the definition of which in the specification (p.22, lines 4-7) is not limiting, the amended claims encompass a method for detecting or quantifying mRNA encoding a polypeptide the expression of which is up-regulated or down-regulated in a prostate cancer, using a polynucleotide, the structure of which is not known, and is unrelated to SEQ ID NO:41, because "selectively hybridizes" encompasses hybridizing under a range of conditions, from very low selective to very high selective conditions, wherein under very low selective conditions, any unrelated polynucleotide sequences would hybridize to SEQ ID NO:41,

2) A sequence at least "80% or 95% identical to SEQ ID NO:41" encompasses variants of SEQ ID NO:41, with unknown structure and function, provided they have 80% or 95% identity with SEQ ID NO:41, in view that there is no disclosure in the specification of any active site or regions responsible for the critical function or biological activity of SEQ ID NO:41, nor is there any disclosure of the biological activity of SEQ ID NO:41, and

3) A nucleic acid "comprising" a sequence "complementary" to SEQ ID NO:41 emcompasses unknown sequences attached to a polynucleotide fragment, which could be as small as a few nucleotides, wherein said fragment is complementary to SEQ ID NO:41, because a complement could be partial or complete complement, wherein a partial complement could be complementary to SEQ ID NO:41, via a few complementary nucleotides.

In view of the above, the specification and the claims clearly fail to describe a polynucleotide that "selectively hybridizes" to a nucleic acid encoding SEQ ID NO:42, the nucleotide sequence SEQ ID NO:41, a sequence at least "80% or 95% identical to SEQ ID NO:41", or a nucleic acid "comprising" a sequence "complementary" to SEQ ID NO:41, by the standards as shown in the examples in Lilly and Enzo.

The specification describes only a single polynucleotide, SEQ ID NO:41. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Thus, the specification does not meet the standards, as shown in the example of Lilly.

Further, the specification does not meet the standards, as shown in the example of Enzo. The specification does not disclose sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

Thus, the specification does not provide an adequate written description of a polynucleotide that "selectively hybridizes" to a sequence "at least 80% or 90% identical" to nucleic acid encoding SEQ ID NO:42, or SEQ ID NO:41, or a sequence "complementary" thereof, that is required to practice the claimed invention.

Since the specification fails to adequately describe the product, it also fails to adequately describe the claimed method using said product.

REJECTION UNDER 35 USC 101, UTILITY, NEW REJECTION

35 U.S.C. 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-3, 6-12, 56-58, 61-67 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, subtantial asserted utility or a well established utility.

Claims 1-3, 6-12, 56-58, 61-67 are drawn to:

A method for detecting or quantitating mRNA encoding a polypeptide the expression of which is up-regulated or down-regulated in a prostate cancer, comprising contacting a biological sample from the patient being tested with a polynucleotide "that selectively hybridizes" to a sequence at least "80% or 95% identical" to a) nucleic acid encoding SEQ ID NO:42, b) nucleic acid comprising SEQ ID NO:41, or c) nucleic acid comprising a sequence complementary to a) or b). The patient is undergoing a therapeutic regimen to treat prostate cancer or is suspected of having prostate cancer.

The specification discloses that Hs.139336 (or AF071202) is a gene that is differentially expressed in prostate tumor tissue compared to normal prostate tissue, using Affymetrix/Eos Hu02 Genechip array (Table 4, p. 138, line 50 and Table 3 on page 121). The specification discloses that RNAs from each prostate tumor are isolated and individual mRNA species is quantified using a custom Affymetrix GeneChip oligonucleotide microarrays, with probes to interrogate approximately 35,000 unique mRNA transcripts (p.97, lines 29-31).

The specification contemplates detection of prostate cancer sequence for diagnostic and therapeutic applications (p.57, last two paragraphs, to pages 61), and treatment of prostate cancer using the prostate cancer modulating protein (p.8).

In the communication of 03/14/05, Applicant asserts that the unigene identifier HS.139336 corresponds to human ATP-binding cassette, subfamily C, member 4, and is set forth in SEQ ID NO:41 (NM-005845) in Table 16 (which was by typographic error labeled as Table 11 on page 302) on page 316 of the specification. Applicant asserts that SEQ ID NO:41 is identified as Hs.139336 in Table 15, at page 297, line 40.

Applicant asserts that Hs.139336 is a gene that is differentially expressed as shown in Tables 3, 4, 5, 6 and 7.

It is noted however that the submitted specification seems to end at page 295, and that tables 15 and 16, although recited in the claims, are not included in the specification.

Thus it is not clear whether SEQ ID NO:41 is the same as Hs.139336 (or AF071202) a human ATP-binding cassette, shown in Tables 3, 4, 5, 6 and 7, and is differentially expressed in prostate tumor tissue compared to normal prostate tissue.

Further, even if SEQ ID NO:41 is the same as Hs.139336 (or AF071202), in the absence of concrete objective evidence, one cannot determine that SEQ ID NO:41 is differentially expressed in prostate tumor tissue compared to normal prostate tissue, in view that only about 35,000 mRNAs transcripts are used in a microarray for quantifying SEQ ID NO:41.

Further experimentation is required to determine what the use is for SEQ ID NO:41, or its encoded protein.

One cannot predict that the screened 35,000 mRNAs transcripts are representative of all mRNAs present in a cell, and consequently, one cannot determine that SEQ ID NO:41 is differentially expressed in prostate tumor tissue compared to normal prostate tissue. A complete cDNA library is one that contains at least one cDNA clone representing each mRNA in a cell, and that there are about 34,000 different types of mRNAs in a mammalian cells and about 500,000 mRNA molecules per cell, as taught in a commonly used text book by Ausubel et al, eds, 1987 (Current protocols in

molecular biology, John Wiley & Sons, New York, p. 5.8.1, under Production of a cDNA library, of record). Ausubel et al further teach that if the number of molecules of the rarest mRNA in a cell is 8, the calculated number of clones that should be screened to achieve a 99% probability that a cDNA will exist in the library is 324,000. Similarly, in another commonly used text book by Sambrook et al, eds, 1989 (Molecular cloning, a Laboratory manuall, 2nd ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, p.8.3-8.7, of record) Sambrook et al teach that a typical mammalian cell contains between 10,000 and 30,000 different mRNA sequences. Sambrook et al further teach that for low abundance mRNAs, i.e. 14 copies/cell, although the minimum clones required to obtain representation of mRNAs of this class is 37,000, but because of preferential cloning of certain sequences, a much larger number of recombinants must be obtained to increase the chances that any given clone will be represented in the library, i. e., about 170,000 clones (p.8.5 last paragraph, bridging p.8.7). Sambrook et al also teach that unfortunately, many mRNAs of interest are present at even lower level, i.e. 1 molecule/cell is not unusual.

Thus based on the teaching in the art, it is clear that one cannot predict that the screened 35,000 mRNA transcripts would be representative of all mRNAs present in a cell. The identification of SEQ ID NO:41 in the selected, incomplete pool of mRNAs transcripts appears to be a serendipitous event. The fact that the claimed polynucleotide is not expressed in one pool of mRNAs transcripts or is expressed in another appears to be an artifact of the analytical system and cannot be extrapolated to a prediction of

whether that molecule is expressed in the tissue "represented" by the pool of mRNAs transcripts.

Neither the specification nor any art of record teaches what SEQ ID NO:41 is, what it does do; they do not teach a relationship to any specific diseases or establish any involvement in the etiology of any specific diseases.

The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polynucleotide. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

1. Specifically, since the claimed invention is not supported by specific, substantial utility or a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

2. If Applicant could overcome the above 101 and 112, first paragraph, **Claims 1-3, 6-12, 56-58, 61-67 are still rejected under 112, first paragraph, because the claims 1-3, 6-12, 56-58, 61-67 encompass a method for detecting or quantifying mRNA encoding a polypeptide the expression of which is up-regulated or down-regulated in a prostate cancer, using a polynucleotide, the structure of which is not known, and is unrelated to SEQ ID NO:41, to detect "a variant of SEQ ID NO:41", the level of expression of which is not predictable, or**

by detecting unknown sequences, that is complementary to SEQ ID NO:41 via a few complementary nucleotides, for reasons already of record in paper of 07/15/05.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

Rejection remains, because the amendment does not address this issue.

1) Due to the language "selectively hybridizes", the definition of which in the specification (p.22, lines 4-7) is not limiting, the amended claims encompass a method for detecting or quantifying mRNA encoding a polypeptide the expression of which is up-regulated or down-regulated in a prostate cancer, using a polynucleotide, the structure of which is not known, and is unrelated to SEQ ID NO:41, because "selectively hybridizes" encompasses hybridizing under a range of conditions, from very low selective to very high selective conditions, wherein under very low selective conditions, any unrelated polynucleotide sequences would hybridize to SEQ ID NO:41,

2) A sequence at least "80% or 95% identical to SEQ ID NO:41" encompasses variants of SEQ ID NO:41, with unknown structure and function, provided they have 80% or 95% identity with SEQ ID NO:41, in view that there is no disclosure in the specification of any active site or regions responsible for the function or biological activity of SEQ ID NO:41, nor is there any disclosure of the biological activity of SEQ ID NO:41, and

3) A nucleic acid "comprising" a sequence "complementary" to SEQ ID NO:41 emcompasses unknown sequences attached to a polynucleotide fragment, which could

be as small as a few nucleotides, wherein said fragment is complementary to SEQ ID NO:41, because a complement could be partial or complete complement, wherein a partial complement could be complementary to SEQ ID NO:41, via a few complementary nucleotides.

One would not known how to make the polynucleotide probes for "selectively hybridizing" to SEQ ID NO:41, or a nucleic acid "comprising" a sequence "complementary" to SEQ ID NO:41, in view that the structure of the polynucleotides for used in the claimed method is not known, and could not be predicted.

Further, one would not known how to use the sequence at least "80% or 95% identical to SEQ ID NO:41" for the claimed method because one cannot predict that these sequences would have similar expression pattern as that of SEQ ID NO:41, in view of the teaching of Schmid et al, Conner et al, all of record, that variants of a wild type do not necessarily express in the same pattern as that of the corresponding wild type.

3. If Applicant could overcome the above 101, and 112, first paragraph rejections, claims 1-3, 6-12, 56-58, 61-67 are still rejected under 112, first paragraph, because the claims 1-3, 6-12, 56-58, 61-67 encompass a method for detecting or quantifying mRNA encoding a polypeptide the expression of which is up-regulated or down-regulated in a prostate cancer, using any biological samples which could be any tissues or any bodily fluid to which the prostate cancer cells have metastasized, for reasons already of record in paper of 07/15/05.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

Rejection remains, because the amendment does not address this issue.

It is unpredictable that the metastasized prostate cancer cells still express SEQ ID NO:41, in view of the teaching in the art that expression of a sequence could be lost during progression toward metastasis (Kibel et al, Zhau et al, Cheung et al, Ren et al, Gingrich et al, all of record).

REJECTION UNDER 35 USC 102

1. Claims 1-3, 7-12, 56-58, 61-67 are rejected under 102(e) as being anticipated by WO 01/60860 A2, for reasons already of record in paper of 07/15/05.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

Rejection remains, because the amendment does not address this issue.

The claimed method seems to be the same as the method taught by WO 01/60860 A2, in view that the sequence taught by WO 01/60860 A2 would selectively hybridize to SEQ ID NO:41.

Although the reference does not specifically teach that the sequence selectively hybridizes to SEQ ID NO:41, or a complement thereof, however, the hybridizing polynucleotide probe for use in the claimed method appears to be the same as the prior

art polynucleotide. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

2. Claims 1-2, 6-8, 12, 56-58, 61-63 are rejected under 102(e) as being anticipated by US 6,329,505 B1, for reasons already of record in paper of 07/15/05.

It is noted that claim 58 was inadvertently omitted from the previous Office action. It is clear that US 6,329,505 B1 teaches detecting the level of mRNA of the sequence in a biological sample, for example, tumor biopsies or tumor tissue (column 36, last two lines, bridging column 37, lines 1-3, and column 46, last paragraph), which reads on a tissue sample in the instant claim 58.

Applicant argues that the amendment renders the rejection moot.

Applicant's arguments in paper of 01/12/06 have been considered but are found not to be persuasive for the following reasons:

Rejection remains, because the amendment does not address this issue.

The claimed method seems to be the same as the method taught by US 6,329,505 B1, because SEQ ID NO:41 seems to be a large fragment, from nucleotide 186 to nucleotide 4162, of the sequence taught by US 6,329,505 B1, and detection of the expression of the sequence taught by US 6,329,505 B1 would inherently detect the expression or the level of the claimed sequence, SEQ ID NO:41.

Further, it is noted that a sequence complementary to SEQ ID NO:41 seems to be the same as the complement of the sequence taught by the art, and thus detection of the expression of the sequence taught by US 6,329,505 B1 would also detect the expression or the level of the complement of SEQ ID NO:41.

Because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MINH TAM DAVIS
March 16, 2006

Susan Ungar
Patent Examiner
Primary